Preclinical studies for a phase 1 clinical trial of autologous hematopoietic stem cell gene therapy for sickle cell disease.

Journal: Cytotherapy

Publication Year: 2017

Authors: Fabrizia Urbinati, Jennifer Wherley, Sabine Geiger, Beatriz Campo Fernandez, Michael L Kaufman, Aaron Cooper, Zulema Romero, Filippo Marchioni, Lilith Reeves, Elizabeth Read, Barbara Nowicki, Elke Grassman, Shivkumar Viswanathan, Xiaoyan Wang, Roger P Hollis, Donald B Kohn

PubMed link: 28733131

Funding Grants: Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease

Public Summary:
WE report the laboratory studies that were done in pre-clinical pharmacology/toxicology and cell processing methods that supported the IND application for the clinical trial of stem cell gene therapy for sickle cell disease.

Scientific Abstract:
BACKGROUND AIMS: Gene therapy by autologous hematopoietic stem cell transplantation (HSCT) represents a new approach to treat sickle cell disease (SCD). Optimization of the manufacture, characterization and testing of the transduced hematopoietic stem cell final cell product (FCP), as well as an in depth in vivo toxicology study, are critical for advancing this approach to clinical trials. METHODS: Data are shown to evaluate and establish the feasibility of isolating, transducing with the Lenti/beta(AS3)-FB vector and cryopreserving CD34(+) cells from human bone marrow (BM) at clinical scale. In vitro and in vivo characterization of the FCP was performed, showing that all the release criteria were successfully met. In vivo toxicology studies were conducted to evaluate potential toxicity of the Lenti/beta(AS3)-FB LV in the context of a murine BM transplant. RESULTS: Primary and secondary transplantation did not reveal any toxicity from the lentiviral vector. Additionally, vector integration site analysis of murine and human BM cells did not show any clonal skewing caused by insertion of the Lenti/beta(AS3)-FB vector in cells from primary and secondary transplanted mice. CONCLUSIONS: We present here a complete protocol, thoroughly optimized to manufacture, characterize and establish safety of a FCP for gene therapy of SCD.

Source URL: https://www.cirm.ca.gov/about-cirm/publications/preclinical-studies-phase-1-clinical-trial-autologous-hematopoietic-stem